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Original article

Frequency of deep vein thrombosis among hospitalized non-surgical Japanese patients with congestive heart failure

Hiroshi Matsuo (MD)[a,*], Makoto Matsumura (MD, FJCC)[b], Yoshie Nakajima (MD)[b,c], Tomohiro Ogawa (MD, PhD)[d], Junichi Tazaki (MD)[e], Takahiro Doi (MD)[e,f], Norikazu Yamada (MD, PhD, FJCC)[g], Takashi Koide (MD)[h], Makoto Mo (MD, PhD)[i], Takeo Suzuki (BP)[j], Nobuaki Sarai (MD, PhD)[j], Hiromu Nakajima (MD, PhD)[j]

[a] *Matsuo Vascular Ultrasound Laboratory, Matsuo Clinic, Suita, Osaka, Japan*
[b] *Department of Cardiology, Saitama Medical University International Medical Center, Hidaka, Saitama, Japan*
[c] *Department of Internal Medicine, Sakado Central Hospital, Sakado, Saitama, Japan*
[d] *Cardiovascular Disease Center, Fukushima Daiichi Hospital, Fukushima, Fukushima, Japan*
[e] *Department of Cardiovascular Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan*
[f] *Department of Clinical Laboratory, Kyoto University Hospital, Kyoto, Kyoto, Japan*
[g] *Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, Tsu, Mie, Japan*
[h] *Department of Cardiology, Takarazuka Municipal Hospital, Takarazuka, Hyogo, Japan*
[i] *Cardiovascular Surgery, Yokohama Minami Kyosai Hospital, Yokohama, Kanagawa, Japan*
[j] *Development & Medical Affairs Division, GlaxoSmithKline K.K., Shibuya, Tokyo, Japan*

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ABSTRACT

Purpose: Congestive heart failure (CHF) is one of the risk factors for deep vein thrombosis (DVT) according to the Japanese guidelines for DVT treatment and prevention. The purpose of this study is to estimate the frequency of DVT among hospitalized CHF patients, since there have been only limited DVT data in Japanese CHF patients.
Methods: Patients enrolled in the study were with risk factors for DVT listed in the guidelines as well as with acute exacerbation of CHF, bed rest for at least 4 days, and aged 60 or above. Patients treated by physical prophylaxis or anti-platelet medication were included, while patients treated by any anticoagulant medicines were excluded. Patients with surgery or injury within 3 months before the hospitalization or diagnosed clinically or with obvious past history as having DVT at hospitalization were excluded. The presence of DVT in the eligible patients was determined by ultrasonography and the images were evaluated by an independent central evaluation committee.
Results: Forty-four patients were enrolled in the study including 19 males and 25 females. The mean age was 79.0 ± 10.6 years, and the mean duration of bed rest was 8.9 ± 3.2 days. Out of these 44 patients, DVT was detected in 15 (34%) patients. Eight patients were on treatment with physical prophylaxis but DVT was still detected in two patients. Furthermore, 12 out of the rest of the patients were treated by anti-platelet agents and were still with DVT in 3 patients.
Conclusion: When evaluated ultrasonographically, the frequency of DVT in hospitalized non-surgical Japanese patients with CHF was approximately 35%. DVT occurred in 25% of patients treated by physical prophylaxis or anti-platelet agents. The results suggest that Japanese hospitalized patients with CHF have a high risk of DVT and thus can be recognized to have potential benefit by preventing and treating DVT according to the guidelines.

Introduction

In Japan, the frequency of deep vein thrombosis (DVT) was recognized as being lower than that overseas [1]. However recent reports suggest that the frequency of DVT in Japanese can be assumed similar to that in Westerners. The frequencies of DVT in

* Corresponding author at: Matsuo Vascular Ultrasound Laboratory, Matsuo Clinic, 16-9 Enoki-cho, Suita 564-0053, Japan. Tel.: +81 6 6388 0041; fax: +81 6 6388 0166.
E-mail address: hiro-matu@fan.hi-ho.ne.jp (H. Matsuo).

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Japanese post-operative patients with hip replacement surgery and knee replacement arthroplasty are 27.4% and 50.0%, respectively [2]. In Westerner, the frequencies are 42–57% for hip replacement surgery and 41–85% for knee replacement arthroplasty [3].

It is recognized that the frequency of VTE in specific patient population of medical practice is higher than that of surgical patients with mild-to-moderate risks, although the reported frequencies have large variance. In some studies outside of Japan, the frequencies of DVT were reported to be 10–26% of general in-hospital patients [4–6]. Especially in patients with CHF, Nicolaides et al. [7] reported the frequency reached to 40%. Based on these studies, the approaches for primary prevention of VTE have already been introduced since more than 20 years ago in USA and Europe. Currently, the requirement of prevention for VTE is widely recognized not only for post-operative patients but also for hospitalized patients in medical practice [8].

The current Japanese prevention guideline [9] recommends primary prevention to some specific internal diseases including congestive heart failure (CHF). Ota et al. [10] reported that NYHA class related to increase in the VTE risk particularly in patients with an extremely high risk for NYHA class IV in Japan. That is the reason why the condition of CHF with NYHA III or IV is targeted by the current prevention guideline for primary prevention. However, as the prevention guideline noted in the introduction, very limited and small-scale studies are available for clarifying the actual frequency of DVT in Japanese non-surgical patients. Since whether there is a benefit to prevent and treat hospitalized CHF patients for DVT has been unclear so far, we aimed to estimate the frequency of DVT in Japanese patients with CHF (NYHA III and IV).

Materials and methods

Before patient enrollment, the protocol had been evaluated and approved by the institutional review board (IRB) or ethical committee (EC) in each medical site. The investigator explained the purpose and methods of the study to the patients and then received his/her signed informed consent (IC) form before conducting any procedures of the study on each patient. The study was conducted by fully following the latest version of the Declaration of Helsinki (2008). The study was fully funded by a sponsor (GlaxoSmithKline, Japan).

This study is a multi-center, prospective, epidemiological study to estimate the frequency of DVT in hospitalized non-surgical Japanese patients with CHF.

Patients enrolled in the study were hospitalized patients identified as at high risk of VTE development based on a combination of risk factors in the prevention guideline. The inclusion criteria were patients with: (a) acute exacerbation of CHF (III or IV of NYHA classification of cardiac performance), (b) bed rest for 4 days and more, and (c) 60 years old or older. The exclusion criteria were patients with: (a) surgery or injury within 3 months before hospitalization, (b) diagnosed clinically or with obvious past history as having DVT at hospitalization, and (c) treated with any anticoagulants. When patients had any underlying diseases (valvular disorder, coronary artery disease, myocardial disorder, atrial fibrillation, atrioventricular block, hypertensive cardiovascular disease, and other diseases) and showed any symptoms related to heart pump dysfunction, they were diagnosed with congestive heart failure. We referred to Framingham criteria of the Framingham study [11] in the diagnosis. We evaluated the severity of heart failure by the NYHA functional classification, but did not investigate the detailed clinical conditions including central venous pressure, left ventricular dimension, left ventricular ejection fraction, and brain natriuretic peptide level in this study. We thus evaluated the occurrence of the DVT by the severity of CHF by using only NYHA classification.

After getting the IC from the patient, the presence of DVT was examined by using lower extremity ultrasonography (US) and the following data were collected.

Collected data

Collected data include demographic variables, life style variables, general medical history, physical examination, current medical condition, lower extremity vein US, and laboratory test (Table 1).

Diagnosis of DVT

Imaging techniques including US, venography, magnetic resonance venography, and contrast enhanced computed tomography have been used for the evaluation of DVT. Among them, diagnosis by US is non-invasive, and has been standardized in the guideline "Criteria for ultrasound diagnosis of deep venous thrombosis of lower extremities" [12] in 2008 by the Japan Society of Ultrasonics in Medicine. We thus considered that diagnosis with US is reproducible and reliable. The training meeting of diagnosis procedure for investigators and medical technologists was implemented before starting the study. The ultrasound diagnosis was performed between the 6th and 14th day of patient's bed rest. If symptomatic

Table 1
Characteristics of patients with congestive heart failure (hospitalized).

Continuous parameters	*N*	Mean (SD)
Age[a] (years)	44	79.1 (10.6)
Body weight (kg)	44	53.3 (16.2)
BMI (kg/m^2)	44	22.5 (6.4)
Systolic blood pressure (mmHg)	44	124.8 (22.5)
Diastolic blood pressure (mmHg)	44	67.4 (16.7)
Duration of rest (days)	44	8.9 (5–16)[b]
Categorical parameters	***N***	**%**
Gender: male/female	19/25	43.2/56.8
Smoking history (male): yes (current or past)/no	9/10	47.4/52.6
Smoking history (female): yes (current or past)/no	2/23	8.0/92.0
Drinking habit (male): yes (current and past)/no	11/8	57.9/42.1
Drinking habit (female): yes (current and past)/no	1/24	4.0/96.0
Fitness habit (male): yes (current and past)/no	2/17	10.5/89.5
Fitness habit (female): yes (current and past)/no	8/17	32.0/68.0
Catheterization within last 3 months: yes/no	11/33	25.0/75.0
Basic disease	44	100.0
Valvular disorder	11	25.0
Coronary artery disease	9	20.5
Myocardial disorder	9	20.5
Atrial fibrillation	5	11.4
Atrioventricular block	4	9.1
Hypertensive cardiovascular disease	2	4.5
Other disease (including multiple diseases)	4	9.1
NYHA classification		
- The stages of heart failure	44	100.0
Class III (moderate)	14	31.8
Class IV (severe)	30	68.2
Physical prevention: yes/no	8/36	18.2/81.8
Medication of antiplatelet agents: yes/no	12/32	27.3/72.7
Medical history of VTE: yes/no	0/44	0.0/100.0
Concomitant disease of malignancy: yes/no	7/37	15.9/84.1
Concomitant disease of diabetes: yes/no	8/36	18.2/81.8
Concomitant disease of dyslipidemia: yes/no	11/33	25.0/75.0
Concomitant disease of hyperuricemia: yes/no	19/25	43.2/56.8
Concomitant disease of hypertension: yes/no	34/10	77.3/22.7
Concomitant disease of angina pectoris: yes/no	11/33	25.0/75.0
Concomitant disease of arrhythmia: yes/no	21/23	47.7/52.3
Concomitant disease of stroke: yes/no	7/37	15.9/84.1

BMI, body mass index; NYHA, New York Heart Association; VTE, venous thromboembolism.

[a] Age: patient's age at the time of ultrasonic examination.

[b] Range (min–max).

DVT was suspected from the patient's signs and symptoms, the test was conducted at that time. The US testing portion of the lower extremity vein was from the ilium to the lower leg; pulmonary thromboembolism was not evaluated in this study.

Diagnosis of new and old thrombus was performed based on stenosis (occlusion or stenosis) and distention (distended or contracted) of veins, floating (free or fixed), regression (none/moderate or severe), consistency (soft or hard), surface character (smooth or irregular), brightness (low/middle or high/middle) and homogeneity (homogeneous or heterogenous) of thrombus, perfusion defect (total or partial), recanalization in thrombus (absent or present), and collateral in branch (absent or present).

The images of the lower extremity vein US and the investigator's evaluations were sent to an independent central evaluation committee. The committee uniformly evaluated and diagnosed the presence of DVT based on these images and information.

Data analysis

The frequency of DVT was calculated by dividing the number of patients with DVT by the number of enrolled patients. Prevalence of potential risk factors for DVT (obesity, bed rest, smoking, diabetes, etc.) was compared between DVT positive and negative groups using Fisher's exact test or Student's *t*-test.

The descriptive statistics for continuous variables show mean ± standard deviation (SD) and frequencies and percentage for categorical variables. The results of the statistical test were indicated by *p* values with significance level of $\alpha = 0.05$.

Results

The study started in September 2009 (first patient enrolled) and ended in August 2010 (last patient enrolled), and was conducted at six medical sites (Fukushima Daiichi Hospital, Saitama Medical University International Medical Center, Yokohama Minami Kyosai Hospital, Mie University Hospital, Kyoto University Hospital, and Takarazuka Municipal Hospital) involving eight principal investigators.

A total of 44 patients were enrolled in the study including 19 males and 25 females, mean age of 79.1 ± 10.6 years, and 14 NYHA-IIIs and 30 NYHA-IVs (Table 1). No patient was prematurely terminated or excluded from the data analysis.

The basic diseases of CHF for the patients were valvular disease ($n = 11$), coronary artery disease ($n = 9$), myocardial disorder ($n = 9$), atrial fibrillation ($n = 5$), atrioventricular block ($n = 4$), hypertensive cardiovascular disease ($n = 2$), and others ($n = 4$). Symptoms observed most commonly among patients were orthopnea, jugular vein, rales, and cardiac dilatation.

The frequency of DVT was 34.1% (15/44) in patients with CHF and its 95% confidence interval was 20.1–48.1%. No statistically significant difference was observed between DVT positive ($n = 15$) and negative ($n = 29$) groups on baseline characteristics of the patients. The details of the characteristics of the patients classified by the presence or absence of DVT are shown in Table 2.

The major results of comparison on prevalence for main important parameters are shown in Table 3. It is notable that DVT development was observed in two (25%) out of 8 patients with physical prophylaxis as well as three (25%) out of 12 patients with antiplatelet medication. Although no significant difference was detected, the mean age of DVT positive group tended to younger than that of DVT negative group (75.1 ± 9.3 vs. 81.1 ± 10.8 years; $p = 0.078$). Six (32%) out of 19 male patients and nine (36%) out of 25 female patients showed DVTs. No difference on DVT development was observed in subgroup analysis for NYHA class (class III vs. IV).

Table 2
Characteristics of patients with congestive heart failure classified by the presence or absence of deep vein thrombosis (DVT).

	DVT (+) ($n = 15$)	DVT (−) ($n = 29$)	*p* value[a]
Male	6 (40.0%)	13 (44.8%)	1.000
Female	9 (60.0%)	16 (55.2%)	
Age (years)	75.1 ± 9.3[b]	81.1 ± 10.8	0.078
Age ≥75 years	9 (60.0%)	21 (72.4%)	0.501
Body weight (kg)	50.4 ± 14.4	54.7 ± 17.2	0.410
BMI (kg/m^2)	21.4 ± 6.4	23.1 ± 6.4	0.404
BMI ≥25 kg/m^2	3 (20.0%)	6 (20.7%)	1.000
Systolic blood pressure (mmHg)	127.2 ± 26.1	123.6 ± 20.8	0.619
Diastolic blood pressure (mmHg)	66.5 ± 12.1	67.8 ± 18.8	0.801
Duration of rest (days)	9.1 ± 3.2	8.789 ± 3.2	0.792
Smoking history (male): yes	3 (20.0%)	6 (20.7%)	1.000
Smoking history (female): yes	1 (6.7%)	1 (3.4%)	1.000
Drinking habit (male): yes	4 (26.7%)	7 (24.1%)	1.000
Drinking habit (female): yes	1 (6.7%)	0 (0.0%)	0.360
Fitness habit: yes	4 (26.7%)	6 (20.7%)	0.714
Catheterization within last 3 months: yes	4 (26.7%)	7 (24.1%)	1.000
NYHA III	7 (46.7%)	7 (24.1%)	0.177
NYHA IV	8 (53.3%)	22 (75.9%)	
Concomitant diseases			
Malignancy	2 (13.3%)	5 (17.2%)	1.000
Chemotherapy for malignancy	1 (6.7%)	2 (6.9%)	1.000
Diabetes	2 (13.3%)	6 (20.7%)	0.695
Dyslipidemia	2 (13.3%)	9 (31.0%)	0.282
Hyperuricemia	6 (40.0%)	13 (44.8%)	1.000
Paralysis	0 (0.0%)	4 (13.8%)	0.282
Hypertension	10 (66.7%)	24 (82.8%)	0.271
Angina pectoris	4(26.7%)	7 (24.1%)	1.000
Myocardial infarction	4(26.7%)	2 (6.9%)	0.159
Thrombophilia	1 (6.7%)	0 (0.0%)	0.341
Arrhythmia	5 (33.3%)	16 (55.2%)	0.102
Heart failure	15 (100%)	29 (100%)	–
Stroke	2 (13.3%)	5 (17.2%)	1.000
Aortic aneurysm	1 (6.7%)	2 (6.9%)	1.000
Varicose vein	0 (0.0%)	0 (0.0%)	–
COPD	2 (13.3%)	1 (3.4%)	0.264
Asthma	0 (0.0%)	2 (6.9%)	0.540
Gastroduodenal ulcer	0 (0.0%)	1 (3.4%)	1.000
Inflammatory bowel disorder	0 (0.0%)	0 (0.0%)	–
Chronic hepatitis	0 (0.0%)	0 (0.0%)	–
Hepatic cirrhosis	0 (0.0%)	1 (3.4%)	1.000
Nephrosis syndrome	1 (6.7%)	1 (3.4%)	1.000
Hormone replacement therapy	0 (0.0%)	0 (0.0%)	–

BMI, body mass index; NYHA, New York Heart Association; COPD, chronic obstructive pulmonary disease.

[a] Statistical testing methods are Fisher's exact test for categorical data and Student's *t*-test for continuous data.

[b] For continuous data, the statistics are presented by mean ± SD.

The summary of DVT conditions of 15 DVT positive patients is listed in Table 4. The 15 DVT positive cases included three (20%) proximal types (including popliteal vein) and three (20%) symptomatic types. New thrombus was detected in 11 (25%) including three with both new and old thrombus. Three patients were treated: two out of 12 asymptomatic patients with unfractionated heparin and warfarin, and one symptomatic out of 3 patients with unfractionated heparin.

D-dimer of the 14 out of 15 patients with DVT was measured at a time point within 2 days of US, and the D-dimer values were higher than the standard cut-off value in all the samples.

Discussion

This study is a multi-center, prospective, epidemiological study to estimate the frequency of DVT in hospitalized non-surgical

Table 3
Results of comparison on prevalence of deep vein thrombosis (DVT) for important parameters.

Categorical parameters

Parameter	Classification	DVT prevalence (%)	*p* value[a]
Gender	Male Female	6/19 (31.6) 9/25 (36.0)	1.000
Age (years)	<75 ≥75	6/14 (42.9) 9/30 (30.0)	0.501
BMI (kg/m^2)	<25 ≥25	12/35 (34.3) 3/9 (33.3)	1.000
Catheterization within last 3 months	Yes No	4/11 (36.4) 11/33 (33.3)	1.000
NYHA classification	Class III Class IV	7/14 (50.0) 8/30 (26.7)	0.177
Physical prevention	Yes No	2/8 (25.0) 13/36 (36.1)	0.695
Antiplatelet agent	Yes No	3/12 (25.0) 12/32 (37.5)	0.500
Concomitant diseases of malignancy	Yes No	2/7 (28.6) 13/37 (35.1)	1.000

Continuous parameters (mean ± SD)

Parameter	DVT (+) (*n* = 15)	DVT (−) (*n* = 29)	*p* value[b]
Age (years)	75.1 ± 9.3	81.1 ± 10.8	0.078
BMI (kg/m^2)	21.4 ± 6.4	23.1 ± 6.4	0.404
Body weight (kg)	50.4 ± 14.4	54.7 ± 17.2	0.410
Systolic blood pressure (mmHg)	127.2 ± 26.1	123.6 ± 20.8	0.619
Diastolic blood pressure (mmHg)	66.5 ± 12.1	67.8 ± 18.8	0.801
Duration of rest (days)	9.1 ± 3.2	8.8 ± 3.2	0.792

BMI, body mass index; NYHA, New York Heart Association.
[a] Fisher's exact test.
[b] Student's *t*-test.

Japanese patients with CHF. Based on the diagnoses of lower extremity vein US, DVTs were identified in 15 patients out of 44 (34.1%; 95% CI, 20.1–48.1%) in non-surgical patients with CHF.

Although the frequency of DVT in Japan has been recognized as being lower than that overseas [1], the overall prevalence of 34.1% and prevalence of newly formed thrombus of 25.0% in Japanese non-surgical patients with CHF are comparable with previously reported prevalence in Western patients; 10–26% of general in-hospital patients [4–6] and 40% in patients with CHF [7]. By using US, thrombus formed approximately within 1 week can be identified as new while that formed 1 week ago or before can be detected as old, and thus most of the newly formed thrombi identified by US may have appeared after starting bed rest at the recruitment for this study. Additionally, some patients developed DVT under physical prophylaxis or anti-platelet medication. Nose et al. [13] reported that popliteal venous flow velocity in the CHF group was significantly attenuated compared to the control group in the resting condition, suggesting that CHF patients have potential risks of DVT. Our result suggests that additional approach including usage of anticoagulant drugs to prevent DVT needs to be considered for hospitalized non-surgical patients with CHF by adhering to DVT prevention guidelines.

In this study, most of the patients with newly formed DVT were not given any treatment. Ten out of 11 patients with new thrombus had distal vein thrombus. The remaining one patient with a new thrombus had proximal vein thrombus, but the proximal end was popliteal vein without symptoms. Based on these conditions of DVT patients, immediate decision for medical intervention was not made by the physicians. In American College of Chest Physicians (ACCP) guideline, regular monitoring of DVT rather than anticoagulant therapy is recommended in patients with acute isolated distal DVT of the leg and without severe symptoms or risk factors for extension [14].

The strength of our study is conducting the standard testing procedure on lower extremity venous US employing a pre-determined operation manual, training of study investigators and laboratory technicians, and central read. This procedure ensured venous US quality and minimized inter-investigating sites' variation. By the standardization of the procedure, US could be a good technique to detect DVT with the advantage of non-invasiveness and low cost over other imaging techniques. In fact, past imaging studies most commonly used US and less frequently venography, CT scan, or MRI [15]. The ACCP guideline for diagnosis of DVT recommends treating DVT and performing no further testing over performing confirmatory venography if the proximal vein is positive by US, and suggests no further testing if DVT is negative by US [15].

No associations between potential risk factors and DVT development were detected. This might be attributed to the limited size of this study. In standard medical practice, most patients with heart diseases including atrial fibrillation, valvular disease, or left ventricular dysfunction received anticoagulation therapy [16,17], and it may be difficult to recruit the patients without treatment with anticoagulation therapy.

Table 4
Summary of deep vein thrombosis (DVT) conditions of 15 DVT positive patients with congestive heart failure.

No.	Location of thrombus	New or old thrombus	Symptoms	D-dimer value (μg/mL)	Treatment
1	Proximal	Old only	None	9.20	None
2	Proximal	Old only	None	5.6	None
3	Proximal	New only	None	19.90	None
4	Distal	Old only	None	1.43	None
5	Distal	Old only	None	7.10	None
6	Distal	New only	None	8.39	None
7	Distal	New only	None	Unmeasured	None
8	Distal	New only	None	2.36	None
9	Distal	New only	None	3.1*	None
10	Distal	New only	None	5.1*	None
11	Distal	New and old	None	15.48	Unfractionated heparin
12	Distal	New only	None	3.5	Warfarin
13	Distal	New and old	Edematous lower limbs, fatigue	15.44	None
14	Distal	New and old	Swollen lower limb	2.79	None
15	Distal	New only	Swollen lower limb, edema, pleural effusion, peritoneal effusion	5.38	Unfractionated heparin

The standard cut-off value of D-dimer is less than 1.0 μg/mL (0.9 μg/mL for two cases with asterisk (*)).

Another limitation of this study would be the profiling of CHF by only NYHA classification. Further study including the profiling of CHF by objective indices including brain natriuretic peptide, ejection fraction and left ventricular end-diastolic dimension, and examination of associations between the objective indices and DVT occurrence may provide with additional information.

In conclusion, the frequency of DVT among Japanese hospitalized CHF patients (34.1%) is comparable to that in Westerners and also to that in Japanese post-operative patients in orthopedics (27.4–50.0%). This study has demonstrated that Japanese hospitalized patients with CHF have a high risk of DVT and thus can be recognized to have potential benefit by preventing and treating DVT according to the guidelines [9].

Conflict of interest

This study was conducted as a sponsored-study of GlaxoSmithKline K.K. with full financial support.

HM and NY are external medical advisors and TS, NS, and HN are employees of GlaxoSmithKline. MMa, YN, TO, JT, TD, TK, and MMo are contracted investigators for this study only. All the authors listed are without any conflict of interest for this study and publication.

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References

[1] Kumasaka N, Sakuma M, Shirato K. Incidence of pulmonary thromboembolism in Japan. Jpn Circ J 1999;63:439–41.
[2] Fujita S, Hirota S, Oda T, Kato Y, Tsukamoto Y, Fuji T. Deep venous thrombosis after total hip or total knee arthroplasty in patients in Japan. Clin Orthop Relat Res 2000;375:168–74.
[3] Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, Colwell CW, American College of Chest Physicians. Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). Chest 2008;133(Suppl. 6):381S–453S.
[4] Samama MM, Cohen AT, Darmon JY, Desjardins L, Eldor A, Janbon C, Leizorovicz A, Nguyen H, Olsson CG, Turpie AG, Weisslinger N, for the Prophylaxis in Medical Patients with Enoxaparin Study Group. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. Prophylaxis in Medical Patients with Enoxaparin Study Group. N Engl J Med 1999;341:793–800.
[5] Mismetti P, Laporte-Simitsidis S, Tardy B, Cucherat M, Buchmüller A, Juillard-Delsart D, Decousus H. Prevention of venous thromboembolism in internal medicine with unfractionated or low-molecular-weight heparins: a meta-analysis of randomised clinical trials. Thromb Haemost 2000;83:14–9.
[6] Geerts WH, Heit JA, Clagett GP, Pineo GF, Colwell CW, Anderson Jr FA, Wheeler HB. Prevention of venous thromboembolism. Chest 2001;119 (Suppl. 1):132S–75S.
[7] Nicolaides AN, Breddin HK, Fareed J, Goldhaber S, Haas S, Hull R, Kalodiki E, Myers K, Samama M, Sasahara A, Cardiovascular Disease Educational and Research Trust and the International Union of Angiology. Prevention of venous thromboembolism. International Consensus Statement. Guidelines compiled in accordance with the scientific evidence. Int Angiol 2001;20: 1–37.
[8] Haas S. Venous thromboembolism in medical patients – the scope of the problem. Semin Thromb Hemost 2003;29(Suppl. 1):17–21 [review].
[9] Editorial Committee on Japanese Guideline for Prevention of Venous Thromboembolism. Japanese Guideline for Prevention of Venous Thromboembolism. Tokyo: Medical Front Int Ltd.; 2004. p. 1–96 [in Japanese].
[10] Ota S, Yamada N, Tsuji A, Ishikura K, Nakamura M, Ito M. Incidence and clinical predictors of deep vein thrombosis inpatients hospitalized with heart failure in Japan. Circ J 2009;73:1513–7.
[11] Mckee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. N Engl J Med 1971;285: 1441–6.
[12] Terminology and Diagnostic Criteria Committee, Japan Society of Ultrasonics in Medicine. Criteria for ultrasound diagnosis of deep venous thrombosis of lower extremities. Jpn J Med Ultrasonics 2008;35:33–6.
[13] Nose Y, Murata K, Wada Y, Tanaka T, Fukagawa Y, Yoshino H, Susa T, Kihara C, Matsuzaki M. The impact of intermittent pneumatic compression devices on deep venous flow velocity in patients with congestive heart failure. J Cardiol 2010;55:384–90.
[14] Guyatt GH, Akl EA, Crowther M, Gutterman DD, Schünemann HJ, for the American College of Chest Physicians Antithrombotic Therapy and Prevention of Thrombosis Panel. Executive Summary Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141: 7S–47S.
[15] Bates SM, Jaeschke R, Stevens SM, Goodacre S, Wells PS, Stevenson MD, Clive Kearon C, Schunemann HJ, Crowther M, Pauker SG, Makdissi R, Guyatt GH. Diagnosis of DVT Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141:e351S–418S.
[16] Yamashita T. Frontiers of anticoaglulation therapy for atrial fibrillation. J Cardiol 2011;58:1–5.
[17] Akao M, Chun Y-H, Wada H, Esato M, Hashimoto T, Abe M, Hasegawa K, Tsuji H, Furuke K. Current status of clinical background of patients with atrial fibrillation in a community-based survey: the Fushimi AF Registry. J Cardiol 2013;61:260–6.